Stories of Hope: Alzheimer's Disease

Dick Mora knew something was happening, but he didn't want to think about it. Whole conversations would vanish from memory as though they never took place. It was frightening.

"We'd gone through quite a bit with my mother who had Alzheimer's disease," he said. "She wouldn't know who I was. So when things started happening to me, I was very, very nervous. I really kind of kept it to myself."

When he was finally diagnosed with Alzheimer's in 2003, the Laguna Niguel man thought it was the beginning of his personal fade to black. "I really believed I was going to be going down like Mother, that I wouldn't know my children, and I wouldn't know my wife."

But Mora, who retired from the pharmaceutical industry, was lucky. His doctor told him about an off-label use of an existing drug to stop the progression of Alzheimer's disease. Now, five years after his diagnosis — an amount of time normally marked by steep cognitive decline — Mora's disease has barely progressed.

"He can still drive a car," said his wife Nancy. "He is very self-sufficient."

"Without aggressive treatment, my life would have been much different," Mora said. "That's why I'm a very strong supporter of research and anything that could bring about a cure for this cruel and unforgiving illness."

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- Read about CIRM funding for Alzheimer's disease

CURING ALZHEIMER'S DISEASE

The mice were old. A t 18 months, they were near the end of their normal lifespan. Worse, the plaques and tangles that signal Alzheimer's Disease ravaged their brains.

Unsurprisingly, their memories were worthless. They could be shown the safe harbor in a water maze — a test of mouse memory — every day and never remember where it was.

Frank LaFerla, Ph.D., director of the Institute for Brain Memory Impairments and Neurological Disorders at the University of California, Irvine, didn't believe stem cells held promise for Alzheimer's patients. But he let experiment decide the question.

LaFerla and his team injected neural stem cells into the hippocampus of the doddering mice. A month later, he put the mice into the water maze where they'd failed so miserably before. This time, the animals learned. They remembered. They performed every bit as well as their Alzheimer's-free peers. But it was puzzling. When LaFerla looked at the brains of the stem-cell treated mice, the diagnostic markers for Alzheimer's disease — amyloid plaques and neurofibrillary tangles — were still there.

“We found absolutely no difference,” LaFerla said. “This is unparalleled. This is the first time in our lab — or probably any lab — we’ve been able to improve Alzheimer’s without lowering plaque pathology. Likewise, we had no effect on tangle pathology.”

Adding to the puzzle, few of the new cells turned into neurons. But when LaFerla looked more closely, he found the brain’s learning center, the hippocampus, had new wiring — a dramatic increase in new connections between neurons, called synapses. The remaining neurons were branching and touching and talking to a greater number of other neurons than they had before the stem cells were injected.

“That was very interesting because the best correlate of cognitive decline is not plaques or tangles, but the degree of synaptic loss,” LaFerla said.

Further studies revealed that the stem cells kicked off this communications revolution by secreting something called brain-derived neurotrophic factor, or BDNF. The stem cells also induced all the surrounding brain cells to squirt more BDNF.

In fact, the researchers were able to inject BDNF into mouse brains and induce synaptogenesis, but at half the level induced by stem cells. This suggests that secreting BDNF is only part of what stem cells do, LaFerla said.

“We got into this not expecting it to work,” he said. “Now we know stem cells don’t need to replace neurons. By implanting stem cells into brains, there is almost a doubling of synaptic density.”

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